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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,796	03/15/2001	Timothy J. Jegla	018512-005010US	6783

20350 7590 04/20/2005

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,796	JEGLA, TIMOTHY J.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-43 and 45-48* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 19 January 2005 under 37 CFR 1.114 based on parent Application No. 09/810,796 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 19 January 2005 has been entered in full. Claims 1-40 are cancelled and claims 41-43 are amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 41-48 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejections to claims 41-48 under 35 U.S.C. § 112, first paragraph (scope of enablement and written description), as set forth at pg 2-11 of the previous Office Action (20 October 2004) are *withdrawn* in view of the amended claims and Applicant's persuasive arguments (19 January 2005). Please see section on 35 U.S.C. § 112, first paragraph below.

Claim Objections

2. Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

3. Claim 48 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or cultured host cell transfected with a vector, does not reasonably provide enablement for a host cell transfected with a vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner has interpreted the claims as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The specification of the instant application teaches that by host cell it is meant "a cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, Hela and the like, e.g., cultured cells, explants, and cells *in vivo*" (pg 25, lines 18-22). However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with the incorporated KCNQ5 potassium channel subunit gene of SEQ ID NO: 1, 2,or 3 is demonstrated to express the peptide. The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to

"intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183).

The specification also discloses that "the present invention provides the nucleic acids of KCNQ5 for the transfection of cells *in vitro* and *in vivo* and that the "nucleic acid for KCNQ, under the control of a promoter, then expresses a KCNQ5 monomer of the present invention, thereby mitigating the effects of absent, partial inactivation, or abnormal expression of the KCNQ5 gene" (pg 50, lines 30-34 through pg 51, lines 1-3). However, the specification does not teach any methods or working examples that indicate a KCNQ5 potassium channel subunit nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification (pg 50-55) is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what specific type of vector would introduce the KCNQ potassium channel subunit nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled

artisan to introduce and express a KCNQ5 potassium channel subunit nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a KCNQ5 nucleic acid in the cell of an organism or be able to produce a KCNQ5 potassium channel subunit protein in that cell.

Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the KCNQ5 potassium channel subunit protein and to introduce and express a KCNQ5 nucleic acid in a cell of an organism for therapy, the lack of direction/guidance presented in the specification regarding how to introduce a KCNQ5 nucleic acid in the cell of an organism to be able produce that KCNQ5, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of making transgenic animals and the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by amending the claim to recite, for example, "An isolated host cell...").

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 41-43 and 45-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Jentsch, T. (U.S. Patent 6,649,371; priority to 60/139,891, filed 6/22/1999).

Jentsch teaches an isolated nucleic acid molecule encoding a polypeptide that comprises an amino acid sequence that is 99.6% identical to SEQ ID NO: 5 of the instant application (see Appendix A attached to the instant Office Action; see nucleotides 1-2691 of SEQ ID NO: 1 of Jentsch and amino acids 1-888 of SEQ ID NO: 5 of the instant application). Jentsch also discloses an isolated nucleic acid molecule encoding a polypeptide that comprises the amino acid sequence of SEQ ID NO: 4 of the instant application (see Appendix B attached to the instant Office Action; see nucleotides 1-2691 of SEQ ID NO: 1 of Jentsch and amino acids 1-897 of SEQ ID NO: 4 of the instant application). Furthermore, Jentsch discloses that the polypeptide encoded by the nucleic acid comprises an alpha subunit of a homomeric potassium channel and an alpha subunit of a heteromeric potassium channel (col 1, lines 54-58; col 4, lines 43-62). Jentsch also teaches an expression vector comprising the nucleic acid molecule encoding the polypeptide and a host cell transfected with the vector (col 13 through col 14, lines 1-16).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Hu et al. U.S. Patent 6,767,736 (the nucleic acid sequences of SEQ ID NO: 1, 3 of Hu et al. are 97.4% similar to SEQ ID NO: 2 of the instant application; the nucleic acid sequences of SEQ ID NO: 1, 3 of Hu et al. are 99.8% similar to SEQ ID NO: 3 of the instant application; the nucleic acid sequence of SEQ ID NO: 3 of Hu et al. is 94.1% similar to SEQ ID NO: 1 of the instant application)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
18 April 2005

Bridget E. Bunner
patent examiner

```
Db       2805 AGCTTGCCTCATGTCAAACTGAAA 2828

RESULT 3
US-09-590-304-1
; Sequence 1, Application US/09590304
; Patent No. 6649371
; GENERAL INFORMATION:
;  APPLICANT: JENTSCH, Thomas
;  TITLE OF INVENTION: NOVEL POTASSIUM CHANNELS AND GENES ENCODING THESE POTASSIUM CHAI
;  FILE REFERENCE: 2815-0136P
;  CURRENT APPLICATION NUMBER: US/09/590,304
;  CURRENT FILING DATE:  2000-06-09
;  NUMBER OF SEQ ID NOS: 10
;  SOFTWARE: PatentIn version 3.0
; SEQ ID NO 1
;   LENGTH: 3137
;   TYPE: DNA
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: CDS
;   LOCATION: (1)..(2691)
US-09-590-304-1

Alignment Scores:
Pred. No.:                0          Length:                3137
Score:                    4527.50    Matches:               887
Percent Similarity:       99.00%     Conservative:          1
Best Local Similarity:    98.89%     Mismatches:            0
Query Match:              99.57%     Indels:                9
DB:                       4          Gaps:                  1

US-09-810-796-5 (1-888) x US-09-590-304-1 (1-3137)

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              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGAAGGATGTGGAGTCGGGCCGGGGCAGGGTGCTGCTGAACTCGGCAGCCGCCAGGGGC 60

Qy         21 AspGlyLeuLeuLeuLeuGlyThrArgAlaAlaThrLeuGlyGlyGlyGlyGlyGlyLeu 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GACGGCCTGCTACTGCTGGGCACCCGCGCGGCCACGCTCGGTGGCGGCGGCGGTGGCCTG 120

Qy         41 ArgGluSerArgArgGlyLysGlnGlyAlaArgMetSerLeuLeuGlyLysProLeuSer 60
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Appendix A (2)

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Qy         81 TyrAsnValLeuGluArgProArgGlyTrpAlaPheIleTyrHisAlaPheValPheLeu 100
Db        241 TACAACGTGCTGGAGAGACCCCGCGGCTGGGCGTTCATCTACCACGCTTTCGTTTTTCTC 300
Qy        101 LeuValPheGlyCysLeuIleLeuSerValPheSerThrIleProGluHisThrLysLeu 120
Db        301 CTTGTCTTTGGTTGCTTGATTTTGTCAGTGTTTTCTACCATCCCTGAGCACACAAAATTG 360
Qy        121 AlaSerSerCysLeuLeuIleLeuGluPheValMetIleValValPheGlyLeuGluPhe 140
Db        361 GCCTCAAGTTGCCTCTTGATCCTGGAGTTCGTGATGATTGTCGTCTTTGGTTTGGAGTTC 420
Qy        141 IleIleArgIleTrpSerAlaGlyCysCysCysArgTyrArgGlyTrpGlnGlyArgLeu 160
Db        421 ATCATTCGAATCTGGTCTGCGGGTTGCTGTTGTCGATATAGAGGATGGCAAGGAAGACTG 480
Qy        161 ArgPheAlaArgLysProPheCysValIleAspThrIleValLeuIleAlaSerIleAla 180
Db        481 AGGTTTGCTCGAAAGCCCTTCTGTGTTATAGATACCATTGTTCTTATCGCTTCAATAGCA 540
Qy        181 ValValSerAlaLysThrGlnGlyAsnIlePheAlaThrSerAlaLeuArgSerLeuArg 200
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Qy        201 PheLeuGlnIleLeuArgMetValArgMetAspArgArgGlyGlyThrTrpLysLeuLeu 220
Db        601 TTCCTACAGATCCTCCGCATGGTGCGCATGGACCGAAGGGGAGGCACTTGGAAATTACTG 660
Qy        221 GlySerValValTyrAlaHisSerLysGluLeuIleThrAlaTrpTyrIleGlyPheLeu 240
Db        661 GGTTCAGTGGTTTATGCTCACAGCAAGGAATTAATCACAGCTTGGTACATAGGATTTTTG 720
Qy        241 ValLeuIlePheSerSerPheLeuValTyrLeuValGluLysAspAlaAsnLysGluPhe 260
Db        721 GTTCTTATTTTTTCGTCTTTCCTTGTCTATCTGGTGGAAAAGGATGCCAATAAAGAGTTT 780
Qy        261 SerThrTyrAlaAspAlaLeuTrpTrpGlyThrIleThrLeuThrThrIleGlyTyrGly 280
Db        781 TCTACATATGCAGATGCTCTCTGGTGGGGCACAATTACATTGACAACTATTGGCTATGGA 840
Qy        281 AspLysThrProLeuThrTrpLeuGlyArgLeuLeuSerAlaGlyPheAlaLeuLeuGly 300
Db        841 GACAAAACTCCCCTAACTTGGCTGGGAAGATTGCTTTCTGCAGGCTTTGCACTCCTTGGC 900
Qy        301 IleSerPhePheAlaLeuProAlaGlyIleLeuGlySerGlyPheAlaLeuLysValGln 320
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Qy        321 GluGlnHisArgGlnLysHisPheGluLysArgArgAsnProAlaAlaAsnLeuIleGln 340
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Qy        361 HisLeuLysAlaLeuHisThrCysSerProThr---------------------------- 371
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Qy        372 AsnGlnLysLeuSerPheLysGluArgValArgMetAlaSerProArgGlyGlnSerIle 391
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Qy        532 GlyLysGlyGlnIleThrSerAspLysLysSerArgGluLysIleThrAlaGluHisGlu 551
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Qy        572 IleGluSerLysLeuAspCysLeuLeuAspIleTyrGlnGlnValLeuArgLysGlySer 591
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Qy        692 IleAsnThrAlaProLysProAlaAlaProThrThrLeuGlnIleProProProLeuPro 711
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Qy        712 AlaIleLysHisLeuProArgProGluThrLeuHisProAsnProAlaGlyLeuGlnGlu 731
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Qy        732 SerIleSerAspValThrThrCysLeuValAlaSerLysGluAsnValGlnValAlaGln 751
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Qy        752 SerAsnLeuThrLysAspArgSerMetArgLysSerPheAspMetGlyGlyGluThrLeu 771
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Tue Apr 5 08:26:18 2005

us-09-810-796-5.

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Qy       792 IleArgSerThrGluGluLeuAsnIleGlnLeuSerGlySerGluSerSerGlySerArg 811
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Qy       812 GlySerGlnAspPheTyrProLysTrpArgGluSerLysLeuPheIleThrAspGluGlu 831
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Qy       832 ValGlyProGluGluThrGluThrAspThrPheAspAlaAlaProGlnProAlaArgGlu 851
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Qy       852 AlaAlaPheAlaSerAspSerLeuArgThrGlyArgSerArgSerSerGlnSerIleCys 871
Db      2581 GCTGCCTTTGCATCAGACTCTCTAAGGACTGGAAGGTCACGATCATCTCAGAGCATTTGT 2640
Qy       872 LysAlaGlyGluSerThrAspAlaLeuSerLeuProHisValLysLeuLys 888
Db      2641 AAGGCAGGAGAAAGTACAGATGCCCTCAGCTTGCCTCATGTCAAACTGAAA 2691
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Appendix B (1)

ALIGNMENTS

RESULT 1
US-09-590-304-1
; Sequence 1, Application US/09590304
; Patent No. 6649371
; GENERAL INFORMATION:
; APPLICANT: JENTSCH, Thomas
; TITLE OF INVENTION: NOVEL POTASSIUM CHANNELS AND GENES ENCODING THESE POTASSIUM CHAN
; FILE REFERENCE: 2815-0136P
; CURRENT APPLICATION NUMBER: US/09/590,304
; CURRENT FILING DATE: 2000-06-09
; NUMBER OF SEQ ID NOS: 10
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 1
; LENGTH: 3137
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: CDS
; LOCATION: (1)..(2691)
US-09-590-304-1

Alignment Scores:	0	Length:	3137
Pred. No.:	4588.00	Matches:	897
Score:	100.00%	Conservative:	0
Percent Similarity:	100.00%	Mismatches:	0
Best Local Similarity:	100.00%	Indels:	0
Query Match:	4	Gaps:	0
DB:			

US-09-810-796-4 (1-897) x US-09-590-304-1 (1-3137)

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Qy         21 AspGlyLeuLeuLeuLeuGlyThrArgAlaAlaThrLeuGlyGlyGlyGlyGlyGlyLeu 40
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Db       121 AGGGAGAGCCGCCGGGGCAAGCAGGGGGCCCGGATGAGCCTGCTGGGGAAGCCGCTCTCT 180
Qy        61 TyrThrSerSerGlnSerCysArgArgAsnValLysTyrArgArgValGlnAsnTyrLeu  80
Db       181 TACACGAGTAGCCAGAGCTGCCGGCGCAACGTCAAGTACCGGCGGGTGCAGAACTACCTG 240
Qy        81 TyrAsnValLeuGluArgProArgGlyTrpAlaPheIleTyrHisAlaPheValPheLeu 100
Db       241 TACAACGTGCTGGAGAGACCCCGCGGCTGGGCGTTCATCTACCACGCTTTCGTTTTTCTC 300
Qy       101 LeuValPheGlyCysLeuIleLeuSerValPheSerThrIleProGluHisThrLysLeu 120
Db       301 CTTGTCTTTGGTTGCTTGATTTTGTCAGTGTTTTCTACCATCCCTGAGCACACAAAATTG 360
Qy       121 AlaSerSerCysLeuLeuIleLeuGluPheValMetIleValValPheGlyLeuGluPhe 140
Db       361 GCCTCAAGTTGCCTCTTGATCCTGGAGTTCGTGATGATTGTCGTCTTTGGTTTGGAGTTC 420
Qy       141 IleIleArgIleTrpSerAlaGlyCysCysCysArgTyrArgGlyTrpGlnGlyArgLeu 160
Db       421 ATCATTCGAATCTGGTCTGCGGGTTGCTGTTGTCGATATAGAGGATGGCAAGGAAGACTG 480
Qy       161 ArgPheAlaArgLysProPheCysValIleAspThrIleValLeuIleAlaSerIleAla 180
Db       481 AGGTTTGCTCGAAAGCCCTTCTGTGTTATAGATACCATTGTTCTTATCGCTTCAATAGCA 540
Qy       181 ValValSerAlaLysThrGlnGlyAsnIlePheAlaThrSerAlaLeuArgSerLeuArg 200
Db       541 GTTGTTTCTGCAAAAACTCAGGGTAATATTTTTGCCACGTCTGCACTCAGAAGTCTCCGT 600
Qy       201 PheLeuGlnIleLeuArgMetValArgMetAspArgArgGlyGlyThrTrpLysLeuLeu 220
Db       601 TTCCTACAGATCCTCCGCATGGTGCGCATGGACCGAAGGGGAGGCACTTGGAAATTACTG 660
Qy       221 GlySerValValTyrAlaHisSerLysGluLeuIleThrAlaTrpTyrIleGlyPheLeu 240
Db       661 GGTTCAGTGGTTTATGCTCACAGCAAGGAATTAATCACAGCTTGGTACATAGGATTTTTG 720
Qy       241 ValLeuIlePheSerSerPheLeuValTyrLeuValGluLysAspAlaAsnLysGluPhe 260
Db       721 GTTCTTATTTTTTCGTCTTTCCTTGTCTATCTGGTGGAAAAGGATGCCAATAAAGAGTTT 780
Qy       261 SerThrTyrAlaAspAlaLeuTrpTrpGlyThrIleThrLeuThrThrIleGlyTyrGly 280
Db       781 TCTACATATGCAGATGCTCTCTGGTGGGGCACAATTACATTGACAACTATTGGCTATGGA 840
Qy       281 AspLysThrProLeuThrTrpLeuGlyArgLeuLeuSerAlaGlyPheAlaLeuLeuGly 300
Db       841 GACAAAACTCCCCTAACTTGGCTGGGAAGATTGCTTTCTGCAGGCTTTGCACTCCTTGGC 900
Qy       301 IleSerPhePheAlaLeuProAlaGlyIleLeuGlySerGlyPheAlaLeuLysValGln 320
Db       901 ATTTCTTTCTTTGCACTTCCTGCCGGCATTCTTGGCTCAGGTTTTGCATTAAAAGTACAA 960
Qy       321 GluGlnHisArgGlnLysHisPheGluLysArgArgAsnProAlaAlaAsnLeuIleGln 340
Db       961 GAACAACACCGCCAGAAACACTTTGAGAAAAGAAGGAACCCAGCTGCCAACCTCATTCAG 1020
Qy       341 CysValTrpArgSerTyrAlaAlaAspGluLysSerValSerIleAlaThrTrpLysPro 360
Db      1021 TGTGTTTGGCGTAGTTACGCAGCTGATGAGAAATCTGTTTCCATTGCAACCTGGAAGCCA 1080
Qy       361 HisLeuLysAlaLeuHisThrCysSerProThrLysLysGluGlnGlyGluAlaSerSer 380
Db      1081 CACTTGAAGGCCTTGCACACCTGCAGCCCTACCAAGAAAGAACAAGGGGAAGCATCAAGC 1140
Qy       381 SerGlnLysLeuSerPheLysGluArgValArgMetAlaSerProArgGlyGlnSerIle 400

Db      1141 AGTCAGAAGCTAAGTTTTAAGGAGCGAGTGCGCATGGCTAGCCCCAGGGGCCAGAGTATT 1200
Qy       401 LysSerArgGlnAlaSerValGlyAspArgArgSerProSerThrAspIleThrAlaGlu 420
Db      1201 AAGAGCCGACAAGCCTCAGTAGGTGACAGGAGGTCCCCAAGCACCGACATCACAGCCGAG 1260
Qy       421 GlySerProThrLysValGlnLysSerTrpSerPheAsnAspArgThrArgPheArgPro 440
Db      1261 GGCAGTCCCACCAAAGTGCAGAAGAGCTGGAGCTTCAACGACCGAACCCGCTTCCGGCCC 1320
Qy       441 SerLeuArgLeuLysSerSerGlnProLysProValIleAspAlaAspThrAlaLeuGly 460
Db      1321 TCGCTGCGCCTCAAAAGTTCTCAGCCAAAACCAGTGATAGATGCTGACACAGCCCTTGGC 1380
Qy       461 ThrAspAspValTyrAspGluLysGlyCysGlnCysAspValSerValGluAspLeuThr 480
Db      1381 ACTGATGATGTATATGATGAAAAAGGATGCCAGTGTGATGTATCAGTGGAAGACCTCACC 1440
Qy       481 ProProLeuLysThrValIleArgAlaIleArgIleMetLysPheHisValAlaLysArg 500
Db      1441 CCACCACTTAAAACTGTCATTCGAGCTATCAGAATTATGAAATTTCATGTTGCAAAACGG 1500
Qy       501 LysPheLysGluThrLeuArgProTyrAspValLysAspValIleGluGlnTyrSerAla 520
Db      1501 AAGTTTAAGGAAACATTACGTCCATATGATGTAAAAGATGTCATTGAACAATATTCTGCT 1560
Qy       521 GlyHisLeuAspMetLeuCysArgIleLysSerLeuGlnThrArgValAspGlnIleLeu 540
Db      1561 GGTCATCTGGACATGTTGTGTAGAATTAAAAGCCTTCAAACACGTGTTGATCAAATTCTT 1620
Qy       541 GlyLysGlyGlnIleThrSerAspLysLysSerArgGluLysIleThrAlaGluHisGlu 560
Db      1621 GGAAAAGGGCAAATCACATCAGATAAGAAGAGCCGAGAGAAAATAACAGCAGAACATGAG 1680
Qy       561 ThrThrAspAspLeuSerMetLeuGlyArgValValLysValGluLysGlnValGlnSer 580
Db      1681 ACCACAGACGATCTCAGTATGCTCGGTCGGGTGGTCAAGGTTGAAAAACAGGTACAGTCC 1740
Qy       581 IleGluSerLysLeuAspCysLeuLeuAspIleTyrGlnGlnValLeuArgLysGlySer 600
Db      1741 ATAGAATCCAAGCTGGACTGCCTACTAGACATCTATCAACAGGTCCTTCGGAAAGGCTCT 1800
Qy       601 AlaSerAlaLeuAlaLeuAlaSerPheGlnIleProProPheGluCysGluGlnThrSer 620
Db      1801 GCCTCAGCCCTCGCTTTGGCTTCATTCCAGATCCCACCTTTTGAATGTGAACAGACATCT 1860
Qy       621 AspTyrGlnSerProValAspSerLysAspLeuSerGlySerAlaGlnAsnSerGlyCys 640
Db      1861 GACTATCAAAGCCCTGTGGATAGCAAAGATCTTTCGGGTTCCGCACAAAACAGTGGCTGC 1920
Qy       641 LeuSerArgSerThrSerAlaAsnIleSerArgGlyLeuGlnPheIleLeuThrProAsn 660
Db      1921 TTATCCAGATCAACTAGTGCCAACATCTCGAGAGGCCTGCAGTTCATTCTGACGCCAAAT 1980
Qy       661 GluPheSerAlaGlnThrPheTyrAlaLeuSerProThrMetHisSerGlnAlaThrGln 680
Db      1981 GAGTTCAGTGCCCAGACTTTCTACGCGCTTAGCCCTACTATGCACAGTCAAGCAACACAG 2040
Qy       681 ValProIleSerGlnSerAspGlySerAlaValAlaAlaThrAsnThrIleAlaAsnGln 700
Db      2041 GTGCCAATTAGTCAAAGCGATGGCTCAGCAGTGGCAGCCACCAACACCATTGCAAACCAA 2100
Qy       701 IleAsnThrAlaProLysProAlaAlaProThrThrLeuGlnIleProProProLeuPro 720
Db      2101 ATAAATACGGCACCCAAGCCAGCAGCCCCAACAACTTTACAGATCCCACCTCCTCTCCCA 2160
Qy       721 AlaIleLysHisLeuProArgProGluThrLeuHisProAsnProAlaGlyLeuGlnGlu 740
Db      2161 GCCATCAAGCATCTGCCCAGGCCAGAAACTCTGCACCCTAACCCTGCAGGCTTACAGGAA 2220
Qy       741 SerIleSerAspValThrThrCysLeuValAlaSerLysGluAsnValGlnValAlaGln 760
Db      2221 AGCATTTCTGACGTCACCACCTGCCTTGTTGCCTCCAAGGAAAATGTTCAGGTTGCACAG 2280
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Appendix B (3).


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Qy       761 SerAsnLeuThrLysAspArgSerMetArgLysSerPheAspMetGlyGlyGluThrLeu 780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2281 TCAAATCTCACCAAGGACCGTTCTATGAGGAAAAGCTTTGACATGGGAGGAGAAACTCTG 2340

Qy       781 LeuSerValCysProMetValProLysAspLeuGlyLysSerLeuSerValGlnAsnLeu 800
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2341 TTGTCTGTCTGTCCCATGGTGCCGAAGGACTTGGGCAAATCTTTGTCTGTGCAAAACCTG 2400

Qy       801 IleArgSerThrGluGluLeuAsnIleGlnLeuSerGlySerGluSerSerGlySerArg 820
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2401 ATCAGGTCGACCGAGGAACTGAATATACAACTTTCAGGGAGTGAGTCAAGTGGCTCCAGA 2460

Qy       821 GlySerGlnAspPheTyrProLysTrpArgGluSerLysLeuPheIleThrAspGluGlu 840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2461 GGCAGCCAAGATTTTTACCCCAAATGGAGGGAATCCAAATTGTTTATAACTGATGAAGAG 2520

Qy       841 ValGlyProGluGluThrGluThrAspThrPheAspAlaAlaProGlnProAlaArgGlu 860
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2521 GTGGGTCCCGAAGAGACAGAGACAGACACTTTTGATGCCGCACCGCAGCCTGCCAGGGAA 2580

Qy       861 AlaAlaPheAlaSerAspSerLeuArgThrGlyArgSerArgSerSerGlnSerIleCys 880
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2581 GCTGCCTTTGCATCAGACTCTCTAAGGACTGGAAGGTCACGATCATCTCAGAGCATTTGT 2640

Qy       881 LysAlaGlyGluSerThrAspAlaLeuSerLeuProHisValLysLeuLys 897
            ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      2641 AAGGCAGGAGAAAGTACAGATGCCCTCAGCTTGCCTCATGTCAAACTGAAA 2691
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